

ADENOVIRUS VECTORS CONTAINING CELL STATUS-SPECIFIC RESPONSE ELEMENTS AND METHODS OF USE THEREOF Inventors: De Chao YU and Daniel R. HENDERSON

- 1. (Once Amended) A replication-competent adenovirus vector comprising an adenovirus gene essential for replication under transcriptional control of a cell status-specific transcriptional regulatory element (TRE).
- 2. The adenovirus vector of claim 1, wherein the adenovirus gene is essential for viral replication.
- 3. The adenovirus vector of claim 2, wherein the adenovirus gene is an early gene.
- 4. The adenovirus vector of claim 2, wherein the adenovirus gene is a late gene.
- 5. The adenovirus vector of claim 3, wherein the adenovirus early gene is E1A.
- 6. The adenovirus vector of claim 3, wherein the adenovirus early gene is E1B.
 - 7. The adenovirus vector of claim 3, wherein the adenovirus early gene is E4.
- 8. The adenovirus vector of claim 1, wherein the cell status-specific TRE is human.
- 9. The adenovirus vector of claim 1, wherein the cell status-specific TRE comprises a hypoxia responsive element (HRE).
- 10. The adenovirus vector of claim 9, wherein the HRE comprises SEQ ID NO:1.

- 11. The adenovirus vector of claim 1, wherein the cell status-specific TRE comprises a cell cycle specific element.
- 12. The adenovirus vector of claim 11, wherein the cell cycle-specific element is from the E2F-1 gene.
- 13. The adenovirus vector of claim 1, wherein the cell status-specific TRE comprises a heat-inducible element.
- 14. The adenovirus vector of claim 1, further comprising a cell type-specific TRE.
- 15. The adenovirus vector of claim 14, wherein the cell type-specific TRE is prostate cell specific.
- 16. The adenovirus vector of claim 15, wherein the prostate cell-specific TRE is a *PSA*-TRE.
- 17. The adenovirus vector of claim 1, further comprising a transgene under transcriptional control of a second cell status-specific TRE.
- 18. (Once Amended) An adenovirus vector comprising an adenovirus gene under transcriptional control of a TRE comprising a cell status-specific TRE and a cell-type specific TRE.
- The adenovirus vector of claim 18, wherein the adenovirus gene is an early gene.
- 20. The adenovirus vector of claim 19, wherein the adenovirus early gene is E1A.
- 21. The adenovirus vector of claim 20, wherein the cell status-specific TRE comprises an HRE and the cell-type specific TRE is a PSA-TRE.

- 22. The adenovirus vector of claim 21, wherein the HRE comprises SEQ ID NO:1 and the PSA-TRE comprises nucleotides about 503 to about 2086 of SEQ ID NO:3 and nucleotides about 5285 to about 5836 of SEQ ID NO:3.
 - 23. A composition comprising an adenovirus vector of claim 1.
- 24. The composition of claim 23, further comprising a pharmaceutically acceptable excipient.
 - 25. A host cell comprising the adenovirus vector of claim 1.
- 26. A method of propagating adenovirus specific for cells which allow a cell status-specific TRE to function, said method comprising combining an adenovirus according to claim 1 with the cells, whereby said adenovirus is propagated.
- 27. A method for conferring selective cytotoxicity on a target cell, said method comprising contacting a cell which allows a cell status-specific TRE to function with an adenovirus vector of claim 1, whereby the vector enters the cell.
- 28. A method for suppressing tumor growth comprising introducing the adenovirus vector of claim 1 into a tumor cell which allows a cell status-specific TRE to function, wherein introduction of the adenovirus vector results in suppression of tumor growth.
- 29. (New) The cell status specific TRE of claim 1 that comprises a cell status specific promoter.
- 30. (New) The cell status specific TRE of claim 1 that comprises a cell status specific enhancer.
- 31. (New) The cell status specific TRE of claim 1 that comprises a cell status specific promoter and a cell status specific enhancer.